CT angiographic detection of cerebral aneurysms in patients with subarachnoid haemorrhage in a South African Institution

By

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Declaration Page

I, Dr Mike Chisha, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicates otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree at this or any other university.

I empower the university to reproduce for research purposes either the whole or any portion of the contents in any manner whatsoever.

Signed by candidate

Mike Chisha, MD

31st December 2019

I dedicate this dissertation to my lovely wife Mary Bwalya Katai – Chisha and my three Children, Samuel Taizya Chisha, Hannah Bwalya Chisha and Uwila Chisha. Thank you for allowing me these couple of years to be away from you so that I could achieve this. It hasn't been easy for us, but this makes it worthwhile. I love you.

Publications and presentations

This work has never been published or presented at any congress.

Abstract

Study rationale

The incidence, location, morphology and size characteristics of cerebral aneurysms in patients presenting to Groote Schuur hospital with either subarachnoid haemorrhage or 3rd nerve palsy have not been established by a formal audit.

Objectives

To determine the patient demographics, frequency of CT angiographic detection of cerebral aneurysms and aneurysmal characteristics in patients presenting to Groote Schuur Hospital with sub-arachnoid haemorrhage and /or 3rd nerve palsy

Materials and methods

Computed tomographic angiographic reports of cerebral vessels of patients who presented either with subarachnoid haemorrhage or 3rd nerve palsy to Groote Schuur hospital were reviewed over a 19-month period from January 2018 – July 2019. The data obtained were coded, entered and analysed using IBM SPSS version 25 software. Descriptive statistics was used to report the means, modes and frequencies. Demographic and aneurysmal data were compared with a similar period 5 years previously.

Results

One hundred and twenty-one aneurysms (121) were analysed in 2018 -2019 and 124 in 2013-2014. The large majority were solitary (92% in both groups), small (94% and 90%) and saccular (96% and 87%) respectively. Significantly more fusiform aneurysms (13% vs 6%) were seen in the earlier group. 8 % of patients had multiple aneurysms. Less than 1% were 'giant' (>20mm). The mean age of the patients was the same for both periods (47 years). The mean aneurysm body size was 5.7mm and 7.1mm and the mean body: neck ratio was

2.1 vs 1.8b).

The most frequent locations were the posterior communicating artery (31.4% [2018/2019], 35% [2013- 2014]), anterior communicating artery (29% [2018/2019], 18.5% [2013/2014]) and the middle Cerebral Arteries (13.2% [2018/2019], 13.7% [2013/2014]). The least common sites were the Superior Cerebellar artery (SCA) [2018/2019] and the Vertebral artery (0.8%) [2013/2014].

Conclusion

This study has compared the demographics of patients presenting to Groote Schuur Hospital with CT angiographically confirmed symptomatic intracranial aneurysms over two periods (January to July) 5 years apart. Both the patient demographics and the aneurysmal architecture were consistent over these time periods. Further our findings conform to that described previously both in Southern Africa and abroad i.e aneurysms which have bled are most commonly related to the posterior communicating, anterior communicating and the middle cerebral arteries and most aneurysms are small and saccular in shape.

Over the periods studied, there was no change in the number of patients presenting to Groote Schuur Hospital for CT cerebral angiography and Interventional treatment post aneurysm rupture. These data represent a baseline for future statistical comparison and the information extrapolated from this study will be useful for interventive planning and resource mobilization at our institution and within the Western Cape Department of Health.

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List of Figures

List of Tables

Abbreviations

ACA: Anterior cerebral artery.

AComm A: Anterior Communicating artery.

BA: Basilar artery.

CTA: Computerised tomography angiogram.

CTCA: Computerised tomography cerebral angiogram.

CT: Computerised Tomography.

ICA: Internal Carotid artery.

MCA: Middle cerebral artery.

PACS: Picture Archiving and Communication System.

P Comm A: Posterior communicating artery.

PICA: Posterior inferior cerebellar artery.

SAH: Subarachnoid Haemorrhage.

SCA: Superior cerebellar artery.

VA: Vertebral artery.

Table of contents

Table of Contents

1. Introduction and Literature review

Intracranial aneurysms occur in about 1 - 10 % of healthy individuals in the world population [1,2,14,24,35].

Their locations and other imaging characteristics vary with about 85% of aneurysms involving the anterior circulation [2]. Most aneurysms are located in the Circle of Willis[2], the most common sites being the anterior communicating artery (25%), followed by the posterior communicating artery (18%) and the bi- /trifurcation of the middle cerebral artery[2].

Cerebral aneurysms can occur at any age but are significantly more common in adults compared to the paediatric population.[2,14,16].

A wide range of factors may be responsible in the formation of intracranial aneurysms. These are discussed below.[14,16]

1.1. Epidemiology of cerebral aneurysms.

About 1 to 10 % of the general population in the world have unruptured intracranial aneurysms[1,2,14,16,24,35].

A fraction (0.25%)[50] of these rupture and result in subarachnoid haemorrhage. The low incidence of SAH compared with the prevalence of unruptured aneurysms is not fully understood. The most important factors predicting rupture include site and size of aneurysm[14,16]. The exact aetiology of intracranial aneurysms remains unclear however factors such as smoking, excessive alcohol consumption, hypertension in addition to familial influence (increased incidence in 1^{st} - 2^{nd} degree relatives with SAH) play a role in aneurysm formation[14] and rupture[48]. Furthermore, several inherited conditions are known to be associated with aneurysm formation. These include Marfan syndrome, adult polycystic kidney disease, Neurofibromatosis type 1, Ehlers-Danlos syndrome types II and IV, Multiple Endocrine Neoplasms type 1, Hereditary Haemorrhagic Telangiectasia and Pseudoxanthoma elasticum[14,16].

The familial occurrence and association with inherited conditions suggest that genetic factors play a role in the development of intracranial aneurysms. Genomic studies in families and sib - pairs with intracranial aneurysms have shown linkage with several loci on chromosomes, particularly chromosomes 1p34.3 –p36.13, 7q11, 19q13.3 and Xp22[14,16].

1.2. Imaging of intracranial/cerebral aneurysms

Angiograms help evaluate the various vascular pathologies within the brain.

Various forms of angiograms are available to image intracranial aneurysms including Multidetector Computed Tomography Angiograms (MDCTA), digital subtraction angiograms (DSA) and magnetic resonance angiograms (MRA).

Multidetector computed tomography angiography is a non-invasive, fast, imaging tool that helps to evaluate vascular pathology. Advances in MDCT technology over the past 3 decades have resulted in MDCTA being equivalent to DSA for the detection of intracranial aneurysms [51,52]. Singh et al[51] [2019] showed that the overall CTA sensitivity in detecting an aneurysm was 96 %. For aneurysms > 4 mm, the sensitivity in detecting aneurysms by a 64 – slice CT detector was 100 % almost equal to DSA[51].

For aneurysms less than 4 mm, the sensitivity is relatively lower. A study by Donmez et al found the sensitivity of detecting aneurysms < 3 mm to be 86.1 % and diagnostic accuracy of 94.1 % and 88.6 %[52]. Singh et al[51] [2019], showed an 83.3 % sensitivity in detecting aneurysms < 4 mm compared to a 100% sensitivity in detecting aneurysms > 4 mm. The Singh study[51] showed an overall sensitivity in detecting aneurysms on per- patient basis to be 96% and that there was no statistically significant difference in the sizes of aneurysms detected between CTA and DSA.

Computed tomographic angiography (CTA) has therefore become a primary diagnostic method for the detection of intracranial aneurysms in cases of subarachnoid haemorrhage who will need neurosurgical intervention[2].

It is advantageous compared with digital subtraction angiography in that it is non-invasive and imaging acquisition takes a few seconds[1,2,13].

In addition to this, two and three-dimensional images can be reconstructed from a single set of raw images and can be viewed on available workstations using with suitable software[15].

The assessment of the cerebral vasculature with CT is more dependent on the technical parameters used than patient dependent.

Since the scanning time is less than 1 minute, the procedure is well tolerated by most patients who have had acute subarachnoid haemorrhage.

Digital subtraction angiography is a fluoroscopic study which primarily aims to image vessels with high image resolution (less than 3 mm). It remains the gold standard especially in imaging intracranial aneurysms less than 3 mm[2,13,51]. The disadvantage of DSA is that it is invasive, expensive, time consuming and may be stressful for both patient and operator[2,14].

Some of the known complications of DSA include; stroke, groin haematoma, intraarterial dissections, intraarterial occlusions, hemiplegia, encephalopathy, death and bronchospasm[49.].

DSA carries a definite but low procedural risk of reversible neurological deficit (i.e. TIA's, reversible stroke) of 0 -2.3% [18, 19] and permanent neurological deficit of 0 – 5 %[18,19,51], hence the need to weigh the risk vs the benefits.

At Groote Schuur Hospital, which is one of the two public referral centres in the Western Cape Province, CT angiography is the first line imaging tool used in diagnosis and evaluation of intracranial aneurysms.

Aneurysm Classification:

Cerebral aneurysms have been classified based on several features which include size in millimetres, shape, aetiology or association with a specific arterial branch[23].

A grading system based on size proposed by B. Pritz [22][2011] grading the aneurysms as small (less than 10 mm), large (11 mm - 25 mm) and giant (more than 25 mm)[25] has been in use. A classification has been developed by the international Study for Unruptured Intracranial Aneurysms [ISUIA] [2003][27.] This classifies aneurysms into four categories: less than 7 mm, 7 to 12 mm, 13 to 24 mm and greater than 25 mm. The risk of aneurysmal rupture is related to an unruptured aneurysm size of greater or equal to 7 mm[39,27-30]. Other factors /parameters which are used to predict aneurysm rupture include meteorological factors (like temperature and atmospheric pressure)[40] as well as morphological factors which include the 'bottleneck factor' (dome/neck ratio)[37], aspect ratio, height/width ratio[37], aneurysmal volume[39] and volume – ostium ratio [39].

Alternative classification systems based on shape (e.g. fusiform and saccular) have been described [22, 32, 33]. Most studies show that aneurysms are more commonly saccular in shape than fusiform. [22,32,33].

Etiological classification includes congenital, acquired, dissecting, infectious and tumor-related[23].

1.3 CT angiography findings in Africa

Very few CT angiographic studies on intracranial aneurysms have been published on the African continent (see - addendum Page 43).

One notable study by Ogeng'o et al[1] [2009] looked at site, age and gender distribution of intracranial aneurysms among Kenyans from 1998 to 2007. In this study intracranial aneurysms commonly affected the posterior communicating artery in young individuals without gender bias[1].

Sabri et al [2011] compared the aneurysmal diagnostic yield of DSA and CTA performed at Inkosi Albert Luthuli Central hospital in KwaZulu/Natal South Africa [2]. This study showed that these imaging modalities were comparable. This study also showed a 5% and 6.5 % greater yield for multiple aneurysms using DSA relative to CTA.

Other studies of aneurysms in South Africa have been digital subtraction angiographic studies by Le Feuvre et al[21], Swartbooi et al[23] and Bignaut et al[24]. Using digital subtraction angiography (DSA), Swartbooi et al., [2016] assessed aneurysmal characteristics and demographics of patients who presented to Universitas Academic Hospital in Bloemfontein over a 6 year period with SAH.[23] In this study, the mean aneurysmal size was 5.8 mm (range of 1.2 -20 mm), with 75 % of aneurysms being smaller than 7 mm[23]. Most patients were women and most aneurysms (72 %) involved the anterior circulation. In their study, the most frequent affected location was the anterior communicating artery [36.7 %][23]. Blignaut et al., [2014] looked at radiological appearances of intracranial aneurysms in HIV positive adults who presented to Universitas Academic Hospital, Bloemfontein with SAH and had confirmed aneurysms on DSA[24]. They found 65.2% had a single aneurysm and 80% had a saccular appearance. 46.7 % of the single aneurysms had a neck width 50% larger than the transverse aneurysm sac size. The mean longitudinal diameter of the aneurysm sac was 4.9 mm and the transverse diameter 4.4 mm[24]. More than 50% of the single aneurysms occurred at the anterior communicating artery[24].

Approximately 35 % of their patients had multiple aneurysms and 50% of these had a complex appearance[24]. A complex aneurysm is defined as an aneurysm that is multilobar or has daughter and/or multi vessel take off configurations[24].

Le Feuvre et al., retrospectively assessed the follow up angiograms of patients who had presented with SAH or 3rd nerve palsies and had berry aneurysms treated between 2002 and 2003 at Groote Schuur Hospital in Cape Town[21]. In their study, 100 % occlusion was achieved in 52% at initial procedure and although only 40/75 (53.3 %) and 34/75 (45.3%) patients attended for 3 month and 1 year follow up angiograms respectively, there was a trend toward progressive thrombosis in 65 % and 82%[21].

1.4. Pathophysiology of aneurysms.

Aneurysmal pathogenesis is related to structural aberrations of the cerebral vasculature. The integrity of the internal elastic lamina is compromised with associated elastic defects in the adjacent layers of the tunica media and adventitia[14].

Defects in the vessel muscles and a reduction of structural support from adjacent structures increases pathology from haemodynamic changes on the arterial wall[14]. Distal aneurysms may be smaller compared with proximal aneurysms, but the risk of rupture may be higher distally[53] due to their relatively thinner parent wall thickness. Carter et al.,[53] noted that intracranial aneurysms in distal locations rarely grew to > 10 mm. They also noted that the average sizes of ruptured intracranial aneurysms were on smaller – sized vessels. They suggested that aneurysms arising from smaller vessels had thinner walls and according to Laplace's law, would experience greater wall tension when subjected to same pressures as intracranial aneurysms with greater wall thickness hence increasing the chance of vessel rupture[53].

The aetiology of cerebral aneurysms remains controversial however a multifactorial aetiology is most likely, reflecting the interaction with environmental factors such as hypertension, Diabetes Mellitus, smoking, atherosclerosis and a congenital predisposition associated with various vascular abnormalities[14,16].

1.5. Management of cerebral aneurysms

Rupture rate of an aneurysm is thought to vary with its size, location and morphological characteristics as well as a patient's personal and family medical history[3]. Management of cerebral aneurysms includes medical care, surgical therapy and endovascular treatment[16]. If aneurysm requires treatment, two primary methods are used: microsurgical clipping or endovascular coiling[3,8,16].

Medical therapy of cerebral aneurysms involves general supportive measures and prevention of complications for individuals who are in the periprocedural period or poor surgical candidates[16]. Treatment is based on the clinical status of the patient, vascular anatomy of the aneurysm, and surgical or endovascular considerations[3,16].

Microsurgical techniques focus on excluding the aneurysm from the cerebral circulation and reducing mass effect on the adjacent structures[3,8, 16.]

Surgical clipping involves performing a craniotomy and placement of a clip on the vessel, excluding a weakened area[22]. Historically a clip may be placed across the aneurysmal neck, preserving the parent vessel and eliminating any aneurysmal rests that may redevelop.

Endovascular coiling has become the treatment of choice of unruptured aneurysms[3,8,16,21].

This treatment strategy requires a high degree of angiographic interventional experience.

At Groote Schuur hospital, endovascular coiling is the treatment of choice for both ruptured and unruptured aneurysms[21].

1.6. This study in context:

Literature on the imaging of intracranial aneurysms in Africa is scanty.

In this study we evaluated the demographics, clinical presentation and imaging findings of patients presenting to Groote Schuur Hospital with confirmed intracranial aneurysms over two 19-month periods (1st January 2018 to 31st July 2019 and 1st January 2013 to 31st July 2014).

2. Aim

The aim of this study was to determine and characterise symptomatic intracranial aneurysm findings on CT angiography in one tertiary referral centre in South Africa.

3. Study Objectives

- To compare the demographics and frequency of CT angiographic detection of cerebral aneurysms in patients presenting to in one tertiary referral centre in the Western Cape (Groote Schuur Hospital) over two periods 5 years apart (2013-2014 and 2018-2019).
- To characterize and compare these CT angiographic appearance of these aneurysms by
  i) Location
  ii) Size
  iii) Shape
  iv) Body to neck ratio (Bottleneck factor)
  v) Multiplicity

4. Methods

We reviewed reports of all computed tomography angiograms (CTA's) of cerebral vessels of patients who presented with subarachnoid haemorrhage and/or 3rd nerve palsy secondary to intracranial aneurysm over a 19-month period from 1st January 2018 to 31st July 2019 and a similar period from 2013 - 2014 using the PACS (Picture and Archiving Communication System) data base at Groote Schuur hospital. The search criteria included using search words such as CTA cerebral vessels, subarachnoid haemorrhage and 3rd nerve palsy on the Groote Schuur hospital radiological information system (RIS) and PACS.

All CTA’s with aneurysms were characterised by aneurysm location (i.e. major cerebral vessel they are arising from), shape (fusiform, berry/saccular) and size using the classification by B Pritz[22] i.e. small (less than 11 mm), large (measuring from 11mm – 25 mm) or giant (measuring more than 25 mm). The data obtained were coded, entered and analysed using IBM SPSS version 25 software. Descriptive statistics was used to report the means, modes and frequencies. The two data sets (2018 -2019 and 2013-2014) were compared.

4.1. Research paradigm

This was a retrospective descriptive cross-sectional comparison of reports of CT cerebral angiograms following spontaneous subarachnoid haemorrhage or presentation with 3rd nerve palsy, over two 19-month periods with an interval period of 41 months.

4.2. Sample

Two study populations were compared: CT cerebral angiograms stored on Groote Schuur Hospital PACS for the above indications between 1st January 2018 to 31st July 2019 and 1st January 2013 to 31st July 2014

4.2.1. Inclusion criteria

All CTCA’s with confirmed aneurysms of patients presenting to GSH with subarachnoid haemorrhage and /or isolated pupil involving 3rd nerve palsy during the period spanning 1st January 2018 to 31st July 2019 and between 1st January 2013 and 31st July 2014 were included in this study.

4.2.2. Exclusion criteria

All patients with technically compromised or inaccessible cerebral CTA's.

Patients presenting with 3rd nerve palsy in whom no aneurysm was detected.

Patients presenting with SAH with no aneurysm detected.

4.3. Materials and Methods

The CTCA's were performed on either a 160-slice Toshiba Aquilion or the 16-slice Siemens Somatom Emotion CT scanners at Groote Schuur Hospital.

The patients were scanned with the standard CTA Head and Neck protocol used at Groote Schuur Hospital:

100 ml Iohexol (Omnipaque) 350 contrast infused via the right upper limb veins i.e. basilic, ulnar or radial veins.

Contrast was injected at 4mls/sec and patients were scanned caudo-cranially from C5 vertebra to vertex.

Barco computer workstations in the Radiology department were used to retrieve all patients' radiological reports from PACS.

Systematic approach:

Our search criteria included using search words such as CTA cerebral vessels, subarachnoid haemorrhage and 3rd nerve palsy on the Groote Schuur hospital radiological information system (RIS) and PACS.

Using the PACS system and the interventional radiology cerebral vessels angiography data base, the CTCA reports for the stated periods were reviewed. All these had been reported at the time of the study by a radiology registrar in training and signed off by a consultant radiologist in the diagnostic radiology department.

Where there was a discrepancy, ambivalence or absence of aneurysm characterisation, the scans were reviewed by the principal investigator (a consultant Neuroradiologist with 20 years of experience and the author, a 5th year resident in diagnostic radiology). Where one or more aneurysms were found, the aneurysm location, size (using the classification by B Pritz[22]), shape and orientation were documented.

4.4. Data collection

Using specific phrases ('subarachnoid haemorrhage',' 3rd nerve palsy' and 'aneurysms') in the radiology reports stored on the Groote Schuur Hospital PACS system (Picture Archiving and Communication System), two data set were obtained: 1st January 2018 to 31st July 2019 and 1st January 2013 to 31st July 2014.

Data were anonymised for confidentiality and recorded in a Microsoft Excel spreadsheet.

The following where highlighted in collected data:

1. Presence of subarachnoid haemorrhage.
2. Presence of one or more cerebral aneurysm(s).
3. Aneurysm location:

    a) Anterior cerebral artery (ACA),

    b) Anterior communicating artery (A Comm A),

    c) Cavernous Internal carotid artery (ICA),

    d) Ophthalmic Internal Carotid artery (ICA)

    e) Posterior communicating artery (P. Comm A),

    f) Posterior cerebral artery (PCA),

    g) Basilar artery (BA)

h) Vertebral artery (VA)

i) Posterior Inferior Cerebellar Artery (PICA)

j) other - specified

4. The absolute size and grading of these aneurysms (using the classification by B Pritz[22]) small (< 10mm), large (11-25mm) and giant (> 25mm).
5. The shape classification of these aneurysms: Fusiform, Saccular, complex
6. Aneurysm body width to neck ratio (Bottleneck factor).
7. Multiplicity of aneurysms.

4.5. Reliability and validity

CTA is now the international standard of care for aneurysm diagnosis. The reports at Groote Schuur hospital are considered reliable as they are all double read (by a registrar with at least one year of CT Head reporting experience and a qualified, certified consultant radiologist.

Where the CTA report was incomplete with respect to aneurysm size, shape, aneurysm body or neck size, the case was reviewed by the investigators.

4.6. Bias

Aneurysm size, shape, neck - body ratio may be affected by aneurysmal rupture.

Parent vessel spasm near the ruptured aneurysm may affect calculation of size ratios, thus possibly leading to bias.

Different CT scanners with different specifications, reconstruction algorithms and measuring software could result in different individual measurements.

5.0. Study Results

2018 -2019 data set:

A total of 112 patients (mean age 47 years), had a total of 121 aneurysms.

The large majority of all aneurysms were in females.

87/112 (78%) patients were female and 25/112 (22) were male.

In this series, 9 patients had multiple aneurysms.

The CTA results showed that 96 % (N=116/121) of the aneurysms were saccular and 4% (N=16/121) were fusiform in shape.

With respect to aneurysmal size, 94.2% (N=114/121) were small, 5% (N=6/121) were large and 0.8% (N=1/121) were giant (Table 1).

During this period, 8% of patients (N=9/112) (7 female and 2 male) had more than 1 aneurysm (multiple aneurysms) where as 92% [103/112] patients had single aneurysms.

Mean aneurysm body size was 5.67 mm and the mean Body: Neck ratio was 1.79 (Tables 1 & 2).

The posterior communicating artery was the most affected artery (31.4%) [38 aneurysms] followed by the anterior communicating artery 28.9% [35 aneurysms] and the middle cerebral artery 13.2 % [16 aneurysms] (Figure 1). The least affected artery was the superior cerebellar artery 0%. (Figure 1)

Most (28.6%) [32/121] aneurysms occurred in the 41 -50 years age group (Figure 2).

2013 – 2014 data set:

113 patients (mean age 47.7 years) had aneurysms

Of these 80 patients (70.8%) were female and 33(29.2%) male.

A total of 124 aneurysms were detected in this group.

87 % (n=108) were saccular and 13% (n=16) fusiform (Table 1).

89.5% (n=111) were classified as small, 7.3% (n=9) as large and 3.2% (n=4) were giant (Table1).

9/113 (8%) patients had multiple aneurysms. (maximum number was 3). Eight (8/9) of these were female, whilst a single male patient had 2 aneurysms.

The mean aneurysm body size was 7.11 mm and the mean body: neck ratio was 2.1.(Tables 1 & 2).

The majority of aneurysms (104/124 [83%]) were single, confined to the Circle of Willis and affecting the anterior circulation. The posterior communicating artery was the most affected artery [34.7%] followed by the anterior communicating artery [18.5%] and the middle cerebral artery [13.7%] (Figure 1). The least affected artery was the VA [0.8%] (Figure 1).

Most aneurysms were found in patients between the ages of 41 -50 years (34.5%) with females being significantly more represented than males in all ages, except in the 13 -30 age group where males outnumbered females by 3:1. Again more females than males were found to have more than one aneurysm.

The least commonly affected vessel was the vertebral artery [0.8%] (2013/2014).

Table 1: Aneurysm shape and size.

	2013 – 2014	2018 – 2019
Aneurysm Shape	Number of aneurysms(n=124)	Number of aneurysms(n=121)
Saccular	108 (86.9%)	116 (95.9%)
Fusiform	16 (13.1%)	5 (4.1%)
Aneurysm Size		
Small (<11mm)	111 (89.5%)	114 (94.2%)
Large (11-25mm)	9 (7.3%)	6 (5%)
Giant (> 25mm)	4 (3.2%)	1 (0.8%)

Figure 1: Site distribution of intracranial aneurysms

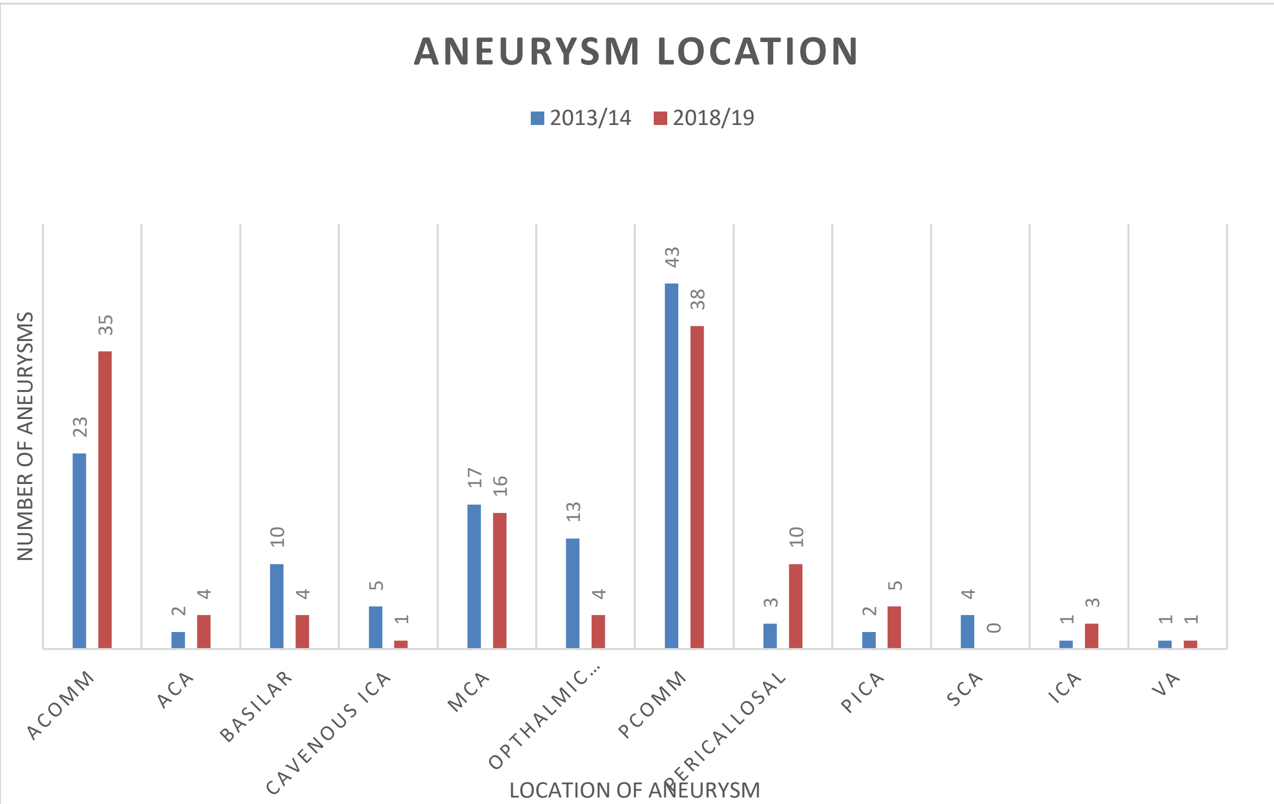


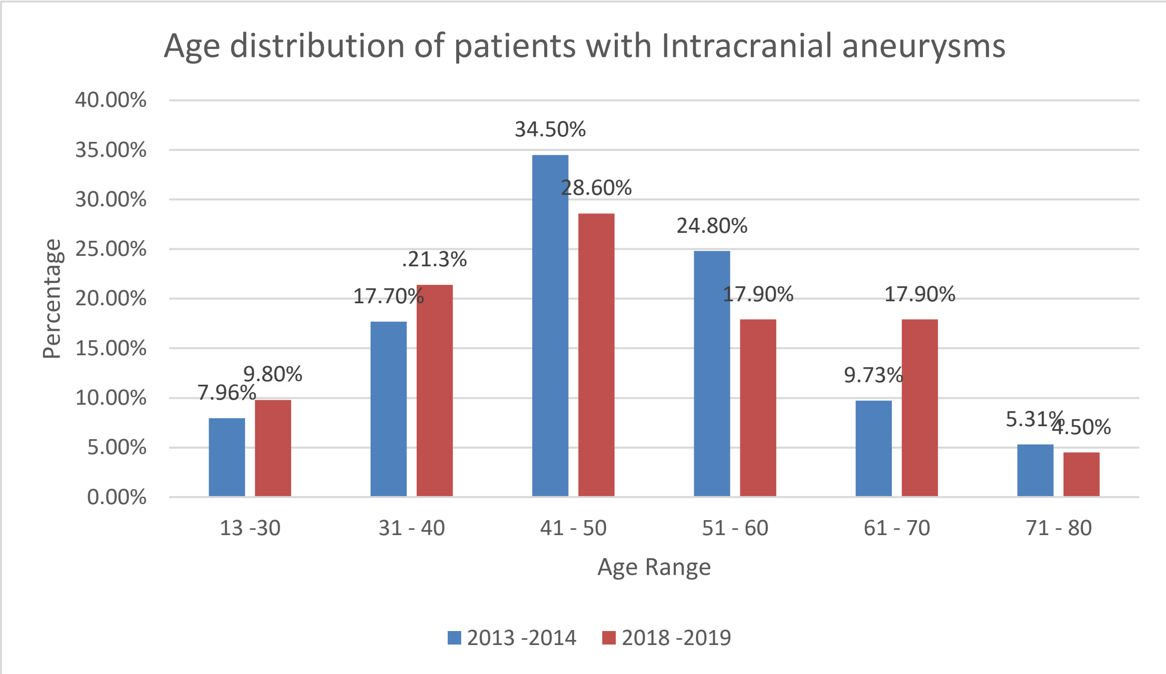
Table 2: Aneurysmal measurements

	N	2013 -2014 Mean(standard deviation)	*n*	2018 – 2019 Mean(standard deviation)	*t*	*P*
Size (mm)	124	7.11 (6.65)	121	5.67(5.14)	1.89	.060
Neck (mm)	124	3.28(2.55)	121	3.19(1.38)	0.31	.756
B/N Ratio	124	2.09(0.84)	121	1.79(0.93)	2.67	.008*

Table 3: Age and Sex distribution of patients with intracranial aneurysms.

Patients age (years)	2013 – 2014			2018 – 2019		
	Total counts	M	F	Total counts	M	F
13 -30	9 (7.96%)	6	3	11 (9.8%)	1	10
31 – 40	20(17.7%)	9	11	24 (21.4%)	5	19
41 – 50	39(34.5%)	5	34	32 (28.6%)	12	20
51 – 60	28(24.8%)	8	20	20 (17.9%)	5	15
61 – 70	11(9.73%)	4	7	20 (17.9%)	1	19
71 – 80	6 (5.31%)	1	5	5 (4.5%)	1	4
TOTAL NUMBER OF PATIENTS	113	33	80	112	25	87

Figure 2: Age distribution of patients with intracranial aneurysms.



6.0 Discussion

The study describes the demographics and CT angiographic findings in two groups of patients presenting to Groote Schuur Hospital with subarachnoid haemorrhage or third nerve palsy due to intracranial aneurysms, 5 years apart.

Most aneurysms were detected in females in the 41 - 50 age group (mean age 47 years) and this was consistent over the two time periods reviewed.

Our results are entirely consistent with previous reports of demographics, size and distribution of intracranial aneurysms both nationally and outside Southern Africa with the large majority observed in the anterior circulation.[1,2,26,41-47]. In our study most were posterior communicating artery aneurysms in both data sets. This pattern has been described elsewhere in South Africa, in Kenya[1] and in an African American population study[44.]

(Sabri et al[2] found aneurysms most commonly in the PComm and AComm arteries.

in their Kwazulu-Natal based study. In Kenya, Ogeng'o et al[1] demonstrated aneurysms in the posterior communicating artery in over a third of cases. The location of the aneurysm determines the presentation and management. For example, a patient with an unbled PComm aneurysm may present with an ipsilateral 3rd nerve palsy requiring endovascular coiling if the body to neck ration is favourable.

Aneurysms were also found in other arteries: (Anterior cerebral , Pericallosal, Superior cerebellar, Posterior cerebral, Ophthalmic division ICA, Cavernous ICA, Supraclinoid ICA, Vertebral artery, Posterior inferior cerebellar artery and Basilar artery) and these are listed in Figure 1. Their distribution does not differ from those previously described in other South African studies [2,23,26].

This probably represents an ethnic diversity in the Western Cape community, or, suggests a different disease pattern in the Western Cape community compared to the communities investigated in other studies. Certainly, factors such as vessel branching pattern, genetic factors and mural factors should also be considered.

Both the 2018 -2019 and 2013 -2014 data showed that aneurysms were predominantly saccular rather than fusiform [Table 1], adding further support to the published literature [22]. Of interest, the proportion of fusiform aneurysms was significantly greater than in a large Korean study where only 22 of 2458 (<1%) were identified as fusiform [55].

Further, there were significantly fewer fusiform aneurysms in the 2018/19 patients compared with the earlier (2013/14) group (p = .013). Fusiform aneurysms are conventionally attributed to atherosclerosis but this is challenged by Park et al who propose that dissection and collagen disease could be responsible for this particular anatomical variant. Intracranial infection in children and in HIV infected adults is associated with vessel wall fragility, destruction of the internal elastic lamina and subadventitial haemorrhage[55]raising the possibility of infectious pathogenesis of these cases.

Further studies are needed to confirm this finding and its implications in our population.

The overwhelming majority of aneurysms are small (<7mm), and this did not differ significantly over the two time periods. (91 % in 2018 -2019 and 89 % in 2013 – 2014).

There was a trend towards smaller aneurysms in 2013/14 compared with 2018/19 (p = .060).

Mean size of aneurysms in 2018 – 2019 was 5.67 mm compared to the mean aneurysmal size from the 2013 – 2014 data (7.11 mm).

The Body/Neck ratio of the aneurysms documented was also significantly smaller in the 2018/19 group (p = 0.008). This trend could suggest changes in treatment/ regimes in diseases such as HIV and hypertension which play a role in the development and rupture of aneurysms. A reduced body/neck ratio is associated with an increased risk of rupture [31,35,36,37,39,] but we have no pre-rupture data for our population so no conclusions can be derived from this finding. Given the low prevalence of SAH in the general population and the high cost of CT angiography, prospective studies would not be feasible in our setting. Given our high prevalence of HIV and Diabetes and Hypertension, however, prospective studies which compare pre-existing clinical conditions with type and size of aneurysm would be of interest.

The frequency of multiple aneurysms was small and stable over time in our study (8%). This is significantly lower than the 35% of HIV positive patients who presented to Universitas Academic Hospital, Bloemfontein with SAH and had multiple aneurysms confirmed on DSA[24]. This study was published by Blignaut et al in 2014. Unfortunately HIV testing is not performed routinely on patients presenting to Groote Schuur Hospital with SAH. It is however tempting to speculate that the national rollout of ARVs subsequent to 2014 may have contributed to this difference.

Multiple aneurysms affecting the female population disproportionately correlates with the literature[2]. [23,26,41 -47].

Multiple aneurysms present commonly in hypertensives, smokers, women and patients with a family history. The prognosis for patients with multiple aneurysms is worse when compared with patients with single aneurysms[38].Given the strong female preponderance for cerebral aneurysm development and rupture generally, as well as the increased rate of HIV in women in the Western Cape, this finding is expected and confirmed in both groups studies.

7.0. Conclusion and Recommendations

This study has compared the demographics of patients presenting to Groote Schuur Hospital with CT angiographically confirmed intracranial aneurysms over two periods 5 years apart. Both the patient demographics and the aneurysmal architecture were consistent over these time periods. Further our findings conform to that described previously both in Southern Africa and abroad: Aneurysms which have bled are most commonly related to the posterior communicating, anterior communicating and the middle cerebral arteries and most bled aneurysms are small (<7mm) and saccular in shape.

We have established that about 6 patients present to GSH for CTA and interventional treatment for cerebral aneurysm rupture per month. This number has been remarkably consistent over the past 5 years. The information extrapolated from this study will be useful for interventive planning and resource allocation at our institution.

The relatively high number of fusiform aneurysms in both groups is of interest and requires further correlation with clinical data. It would be of particular interest to establish the immune status of these patients. Questions raised by this study could be addressed in future research opportunities. The role of HIV and correlation with CD4 and viral count being one important example.

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Appendix A – 1: Ethics Clearance Certificate

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

28 November 2019

HREC REF: 775/2019

Prof S. Candy
Department of Radiation Oncology
C-16
NGSH

Dear Prof Candy

PROJECT TITLE: CT ANGIOGRAPHIC DETECTION OF CEREBRAL ANEURYSMS IN PATIENTS PRESENTING WITH SUBARACHNOID HAEMORRHAGE IN A SOUTH AFRICAN INSTITUTION. (MMED DEGREE - MIKE CHISHA)

Thank you for submitting your response to the concerns raised by the Faculty of Health Sciences Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 November 2020.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period. (Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledges that the student: Mike Chisha will also be involved in this study.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC REF in all your correspondence

Yours sincerely

Signature Removed

PROFESSOR MARC BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
NHREC-registration number: REC-210208-007

HREC/ref: 775/2019

Appendix A – 2: Groote Schuur Hospital research approval

Western Cape Government

Health

GROOTE SCHUUR HOSPITAL

Enquiries: Dr Bernadette Eick
e-mail: Bernadette.Eick@westerncape.gov.za

Professor Sally Candy
RADIATION ONCOLOGY

E-mail: Sally.Candy@uct.ac.cza / mikechisha@yahoo.com

Dear Professor Candy,

RESEARCH PROJECT: CT Angiographic Detection of Cerebral Aneurysms In Patients Presenting With Subarachnoid Haemorrahage in A South African Institution (MMed Dr Mike Chisha)

Your recent letter to the hospital refers.

You are granted permission to proceed with your research, which is valid until **30 November 2020.**

Please note the following:

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) No additional costs to the hospital should be incurred i.e. Lab, consumables or stationary. **If access to TRACK Care/NHLS is required, kindly attach our letter of approval to the application form.**
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Pease provide the research assistant/field worker with a copy of this letter as verification of approval.
f) Confidentiality must always be maintained .
g) **Should you at any time require photographs of your subjects, please obtain the necessary indemnity forms from our Public Relations Office (E45 OMB or ext. 2187/2188).**
h) Should you require additional research time beyond the stipulated expiry date, please apply for an extension.
i) Pease discuss the study with the HOD before commencing.
j) Pease introduce yourself to the person in charge of an area before commencing.
k) On completion of your research, please forward any recommendations/findings that can be beneficial to use to take further action that may inform redevelopment of future policy / review guidelines.
l) **Kindly submit a copy of the publication or report to this office on completion of the research.**
m) **At no time should any posters encouraging patients to partake in research, be displayed within a clinical area.**

I would like to wish you every success with the project.

Yours sincerely

Signature Removed

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER
Date: 11 December 2019

C.C. Mr. L. Naidoo
Dr H. Aziz
Professor J. Parkes

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ADDENDUM A: Most frequent site of aneurysm (ethnic groups)

Author	Population	Sample size	Most frequent
Sabri et al., 2011[a]	South African	277	Posterior Communicating artery
Coert de Vries et al., 2014[a]	South African	23	Anterior communicating artery
Ogeng'o, et al., 2009[b]	Kenyan	58	Posterior communicating artery
Louw, et al., 2004[c]	South African	223	Internal carotid artery
Krishna et al.,2005[d]	Indian	451	Anterior communicating artery
Sim, et al., 2004[f]	Korean	2500	Anterior communicating artery
Firouznia et al., 2005[g]	Iranian	130	Anterior Communicating artery
Oh et al., 2008[h]	Polish	17	Internal Carotid artery
Ohaegbulam et al., 1990[g]	American(black)	73	Posterior communicating artery
	American(white)	171	Middle Cerebral artery Anterior cerebral artery
Anim, 1985[i]	Ghanaian	310	Anterior Cerebral artery